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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,052	08/19/2003	Arthur M. Krieg	C1037.70048US00	4791

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EXAMINER	
ARCHIE, NINA	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,052	KRIEG ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,12-17,22,24-28,32,36,39,44,46,48,49,66,67 and 95-99* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,12,14,16,17,22,24,26,27,49,66,67,97,98 and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 3-5,13,15,23,25,28,32,36,39,44,46,48,66,70,88,94-96 and 99.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :11/19/2004, 3/17/2004, 8/5/2005, 10/3/2005.

DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

2. The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

3. The information disclosure statement filed on 11/19/2004, 3/17/2004, 8/5/2005, 10/3/2005 has been considered. Initialed copies are enclosed.

Election/Restrictions

4. Applicant's election of Group I claims 1-5, 12-17, 22, 24-28, 32, 36, 39, 44, 46, 48-49, 66-67, 95-99 are acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3-5, and 13, 15, 23, 25, 28, 32, 36, 39, 44, 46, 48, 66, 70, 88, 94-96 and 99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group II (claim 23), Group III (claim 70), Group IV (claim 88), Group V (claim 94) or a nonelected species (claim 3-5, 13, 15, 25, 28, 32, 36, 39, 44, 46, 48, 66, 95-96, 99), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in reply filed on 8/2/2006.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claim 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 of U.S. Application No. 11/361,313.

In the instant case, the claim 49 is drawn to an oligonucleotide comprising: an octameric sequence comprising at least one YZ dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage, and at least 4T nucleotides, wherein Y is a pyrimidine or modified pyrimidine, wherein Z is a guanosine or modified guanosine, and wherein the oligonucleotide includes at lest one stabilized internucleotide linkage.

U.S. Application No. 11/361,313 claim 1 are drawn to an oligonucleotide of 3 to 24 nucleotides in length comprising at least one YZ dinucleotide with a phosphodiester or phosphodiester-like internucleotide linkage, and at least 4 T nucleotides, wherein Y is a nucleotide comprising a pyrimidine or modified pyrimidine base, wherein Z is a nucleotide comprising a guanine or modified guanine, and wherein the oligonucleotide includes at least one stabilized internucleotide linkage.

Although the conflicting claims are not identical, they are not patentably distinct. The U.S. Application No. 11/361,313 recites the "oligonucleotide". The species of the olignucleotide anticipate the genus claims of any oligonucleotide.

Thus, claim 49 encompassing the oligonucleotide in the present application is obvious over claims 1 of U.S. Application No. 11/361,313.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-2, 12, 14, 16-17, 22, 24, 26-27, 49, 66-67, 97-98, and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Krieg et al WO/01/22972A2.

Claims 1-2, 12, 14, 16-17, 22, 24, 26-27, 49, 66-67, 97-98, and 100 are drawn to an immunostimulatory nucleic acid molecule having at least one internal pyrimidine-purine (YZ) dinucleotide and a chimeric backbone, wherein the at least one internal YZ dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, wherein optionally each additional internal YZ dinucleotide has a phosphodiester, phosphodiester-like, or stabilized internucleotide linkage, and wherein all other internucleotide linkages are stabilized (claim 1); an oligonucleotide comprising an octameric sequence comprising at least one YZ dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage, and at least 4 T nucleotides, wherein Y is a pyrimidine or modified pyrimidine, wherein Z is a guanosine

or modified guanosine, and wherein the oligonucleotide includes at least one stabilized internucleotide linkage (claim 49); an oligonucleotide comprising 5'GNC 3', wherein N is a nucleic aid sequence of 4-10 nucleotides in length and is at least 50% T and does not include a CG dinucleotide, and the oligonucleotide includes at least one stabilized internucleotide linkage (claim 67); an oligonucleotide comprising N_1-C_G-N_2-C_G-N_3 wherein N_1 and N_3 are each independently a nucleic acid sequence 1-20 nucleotides in length, wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide linkage, wherein N2 is independently a nucleic acid sequence 4-20 nucleotides in length, and wherein G-N_2-C includes at least 5 stabilized linkages (claim 97); an oligonucleotide comprising N_1-C_G-N_2-C_G-$N_3$3 wherein N_1, N_2, and N_3 are each independently a nucleic acid sequence of 0-20 nucleotides in length and wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide linkage, wherein the oligonucleotide is not an antisense oligonucleotide, triple-helix-forming oligonucleotide, or ribozyme (claim 98).

Krieg et al teaches an immunostimulatory nucleic acid molecule having at least one internal pyrimidine-purine (YZ) dinucleotide and a chimeric backbone, wherein the at least one internal YZ dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, wherein optionally each additional internal YZ dinucleotide has a phosphodiester, phosphodiester-like, or stabilized internucleotide linkage, and wherein all other internucleotide linkages are stabilized, wherein the immunostimulatory nucleic acid comprises a plurality of internal YG dinucleotides having a phosphodiester or phosphodiester-like internucleotide linkage, wherein the at least one internal YG dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage is CG, wherein the immunostimulatory nucleic acid molecule is a B-Class immunostimulatory nucleic acid molecule, wherein the immunostimulatory nucleic acid molecule is 4-100 nucleotides long, wherein the immunostimulatory nucleic acid molecule is not an antisense oligonucleotide, triple-helix-forming oligonucleotide, or ribozyme, wherein the nucleic acid has a backbone comprising deoxyribose or ribose, wherein the phosphodiester or phosphodiester-like internucleotide linkage is

phosphodiester, wherein the stabilized internucleotide linkages are selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, methylphosphorothioate, and any combination thereof, wherein the stabilized internucleotide linkages are phosphorothioate (see abstract, pgs. 2-12, pgs. 18-24, pgs. 27-30, pg. 34, pgs. 36-37).

Krieg et al teaches an oligonucleotide comprising an octameric sequence comprising at least one YZ dinucleotide having a phosphodiester or phosphodiester-like internucleotide linkage, and at least 4 T nucleotides, wherein Y is a pyrimidine or modified pyrimidine, wherein Z is a guanosine or modified guanosine, and wherein the oligonucleotide includes at least one stabilized internucleotide linkage. Krieg et al teaches an oligonucleotide comprising 5'GNC 3', wherein N is a nucleic aid sequence of 4-10 nucleotides in length and is at least 50% T and does not include a CG dinucleotide, and the oligonucleotide includes at least one stabilized internucleotide linkage. Krieg et al teaches an oligonucleotide comprising N_1-C_G-N_2-C_G-N_3 wherein N_1 and N_3 are each independently a nucleic acid sequence 1-20 nucleotides in length, wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide linkage, wherein N2 is independently a nucleic acid sequence 4-20 nucleotides in length, and wherein G-N_2-C includes at least 5 stabilized linkages. Krieg et al teaches an oligonucleotide comprising N_1-C_G-N_2-C_G-$N_3$3 wherein N_1, N_2, and N_3 are each independently a nucleic acid sequence of 0-20 nucleotides in length and wherein _ indicates an internal phosphodiester or phosphodiester-like internucleotide linkage, wherein the oligonucleotide is not an antisense oligonucleotide, triple-helix-forming oligonucleotide, or ribozyme (see abstract, pgs. 2-12, pgs. 18-24, pgs. 27-30, pg. 34, pgs. 36-37).

Krieg et al teaches that the immunostimulatory nucleic acid may be any size (i. e., length) provided it is at least 4 nucleotides, in important embodiments; the immunostimulatory nucleic acids have a length in the range of between 6 and 100. In still other embodiments, the length is in the range of between 8 and 35 nucleotides. Preferably, the TG oligonucleotides range in size from 15 to 25 nucleotides. Krieg et al

teaches the size (i. e., the number of nucleotide residues along the length of the nucleic acid) of the immunostimulatory nucleic acid may also contribute to the stimulatory activity of the nucleic acid. Krieg et al teach that it has been discovered, surprisingly that even for highly immune stimulating immunostimulatory nucleic acids, the length of the nucleic acid influences the extent of immunostimulation that can be achieved and it has been demonstrated that increasing the length of a T-rich nucleic acid up to 24 nucleotides causes increased immune stimulation. Krieg et al teaches that the experiments presented in the examples demonstrate that when the length of the T-rich nucleic acid is increased from 18 to 27 nucleotides the ability of the nucleic acid to stimulate an immune response is increased significantly (compare ODN #2194, 2183,2195, and 2196 decreasing in size from 27-18 nucleotides). Krieg et al teaches that that increasing the length of the nucleic acid up to 30 nucleotides had a dramatic impact on the biological properties of the nucleic acid but increasing the length beyond 30 nucleotides did not appear to further influence the immune stimulatory effect (e. g., compare ODN 2179 to 2006) (see pgs. 28-29).

Krieg et al teach that TG nucleic acids ranging in length from 15 to 25 nucleotides in length may exhibit an increased immune stimulation thus, in one aspect, the invention provides an oligonucleotide that is 15-27 nucleotides in length (i. e., an oligonucleotide that is 15,16,17,18,19,20,21,22,23,24,25,26 or 27 nucleotides in length) that may be a T-rich nucleic acid or may be a TG nucleic acid, or may be both a T-rich and a TG nucleic acid. In one embodiment, the oligonucleotide is not a T-rich nucleic acid nor is it a TG nucleic acid. In other embodiments, the oligonucleotide does not have a CG motif. Krieg et al teach that the invention similarly provides oligonucleotides that are 15-27 nucleotides in length, oligonucleotides that are 18-25 nucleotides in length, oligonucleotides that are 20-23 nucleotides in length, and oligonucleotides that are 23- 25 nucleotides in length and any of the foregoing embodiments relating to oligonucleotides 15-27 in length also relate to the oligonucleotides of these differing lengths (see pgs 28-29).

Krieg et al teach that for facilitating uptake into cells immunostimulatory nucleic acids preferably have a minimum length of 6 nucleotide residues. Krieg et al teach that nucleic acids of any size greater than 6 nucleotides (even many kb long) are capable of inducing an immune response according to the invention if sufficient immunostimulatory motifs are present, since larger nucleic acids are degraded inside of cells and preferably the immunostimulatory nucleic acids are in the range of between 8 and 100 and in some embodiments T-rich containing immunostimulatory nucleic acids are between 24 and 40 nucleotides in length and TG containing immunostimulatory nucleic acids are between 15 and 25 nucleotides in length (see pgs 28-29).

Krieg et al teaches an olignucleotide comprising an oligonucleotide comprising: 5'T*C_G(N_6C_G N_7)$_{2-3}$T*C_G*T*T3' wherein N_6 and N_7 are independently between 1 and 5 nucleotides in length, and optionally N_6 is one nucleotide, preferably T or A and optionally N_7 is five nucleotides, preferably five pyrimidines or TTTTG wherein * refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and wherein the oligonucleotide has a length of 16-40 nucleotides, wherein the oligonucleotide has the following structure: 5' T*C G*T*C G*T*T*T*T*T*G*A*C G*T*T*T*T*T*G*T*C 'G*T*T 3' (SEQ ID NO: 313) (see abstract, pgs. 2-12, pgs. 18-24, pgs. 27-30, pg. 34, pgs. 36-37).
STIC Sequence Search Results SEQ ID NO: 331).

Status of the Claims

7. No claims are allowed.

Claims 1-2, 12, 14, 16-17, 22, 24, 26-27, 49, 66-67, 97-98, and 100 are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER